

Claims

1. A method of treating or preventing a condition of excessive cell death in a subject, said method comprising administering to said subject a soluble CPG15 (s-CPG15) compound having s-CPG15 biological activity in an amount and for a time
5 sufficient to prevent, reduce, or eliminate the symptoms of said condition.

2. The method of claim 1, wherein said s-CPG15 lacks either a signal sequence or a GPI linkage sequence

10 3. The method of claim 2, wherein said s-CPG15 lacks a signal sequence and a GPI linkage sequence.

4. The method of claim 3, wherein said soluble CPG15 lacking a signal sequence and a GPI linkage sequence has the *in vitro* biological activity of a CPG15
15 protein wherein

- a) the signal sequence and the GPI linkage sequence of said CPG15 protein have been cleaved;
- b) said CPG15 protein has been bound to a cell membrane; and
- c) said CPG15 protein has been released from the cell.

20

5. The method of claim 3, wherein said s-CPG15 comprises the sequence of SEQ ID NO: 1.

6. The method of claim 3, wherein said s-CPG15 comprises a post-
25 translational modification.

7. The method of claim 6, wherein said post-translational modification comprises the attachment of a membrane component to said s-CPG15.

8. A method of reducing or preventing cell death, said method comprising administering to a cell s-CPG15 in an amount and for a time sufficient to reduce or prevent said cell death.

5 9. The method of claim 8, wherein said s-CPG15 lacks either a signal sequence or a GPI linkage sequence

10. The method of claim 9, wherein said s-CPG15 lacks a signal sequence and a GPI linkage sequence.

10 11. The method of claim 10, wherein said soluble CPG15 lacking a signal sequence and a GPI linkage sequence has the *in vitro* biological activity of a CPG15 protein wherein

- 15 a) the signal sequence and the GPI linkage sequence of said CPG15 protein have been cleaved;
- b) said CPG15 protein has been bound to a cell membrane; and
- c) said CPG15 protein has been released from the cell.

20 12. A method of promoting the survival or differentiation of a cell comprising administering to said cell s-CPG15 for a time and in an amount to promote the survival or differentiation of said cell.

25 13. The method of claim 12, wherein said soluble CPG15 lacking a signal sequence and a GPI linkage sequence has the *in vitro* biological activity of a CPG15 protein wherein

- a) the signal sequence and the GPI linkage sequence of said CPG15 protein have been cleaved;
- b) said CPG15 protein has been bound to a cell membrane; and
- c) said CPG15 protein has been released from the cell.

14. The method of claim 12, wherein said survival or differentiation of said cell is increased by at least 5% as compared to a control cell not treated by said method.

5 15. A composition of matter comprising a purified polypeptide having s-CPG15 biological activity.

16. The composition of claim 15, wherein said s-CPG15 lacks either a signal sequence or a GPI linkage sequence

10 17. The composition of claim 16, wherein said s-CPG15 lacks a signal sequence and a GPI linkage sequence.

18. The composition of claim 17, wherein said soluble CPG15 lacking a
15 signal sequence and a GPI linkage sequence has the *in vitro* biological activity of a CPG15 protein wherein

a) the signal sequence and the GPI linkage sequence of said CPG15 protein have been cleaved;

b) said CPG15 protein has been bound to a cell membrane; and

20 c) said CPG15 protein has been released from the cell.

19. The composition of claim 17, wherein said s-CPG15 comprises the sequence of SEQ ID NO: 1.

25 20. The composition of claim 17, wherein said s-CPG15 comprises a post-translational modification.

21. A method of treating or preventing a condition of undesirable cell survival in a subject, said method comprising administering to said subject a purified antibody or antigen-binding fragment that specifically binds a polypeptide having s-CPG15 biological activity, wherein said administering is in an amount and for a time
5 sufficient to prevent, reduce, or eliminate the symptoms of said condition.

22. The method of claim 21, wherein said condition is selected from the group consisting of cancer, tumor-associated angiogenesis, or immune system conditions.

10 23. A method of treating or preventing a condition of undesirable cell survival in a subject, said method comprising administering to said subject a double-stranded RNA that is complementary to an mRNA sequence encoding a protein having s-CPG15 biological activity, wherein said administering is sufficient to reduce or inhibit the expression of s-CPG15.

15 24. The method of claim 23, wherein said condition is selected from the group consisting of cancer, tumor-associated angiogenesis, or immune system conditions.

25 25. The method of claim 23, wherein said double-stranded RNA is processed into small interfering RNAs (siRNAs) 19 to 25 nucleotides in length.

26. The method of claim 23, wherein said double stranded RNA is made from a short hairpin RNA (shRNA).

25 27. The method of claim 26, wherein said shRNA comprises the sequence of SEQ ID NO: 2.

28. The method of claim 26, wherein said shRNA comprises the sequence of SEQ ID NO: 3.

29. A method of treating or preventing a condition of undesirable cell survival in a subject, said method comprising administering to said subject a nucleic acid encoding a truncated form of CPG15, wherein said administering is sufficient to reduce or inhibit the biological activity of s-CPG15.

30. The method of claim 29, wherein said condition is selected from the group consisting of cancer, tumor-associated angiogenesis, or immune system conditions.

31. A method of treating or preventing a condition of undesirable cell survival in a subject, said method comprising administering to said subject a compound comprising a truncated form of CPG15 protein, wherein said administering is sufficient to reduce or inhibit the biological activity of s-CPG15.

32. The method of any one of claims 21, 23, 29, and 31, wherein said undesirable cell survival is reduced by at least 5%.

33. A method of enhancing cell death, said method comprising administering to a cell an antibody or antigen-binding fragment that specifically binds s-CPG15.

34. A method of enhancing cell death, said method comprising administering to a cell a double-stranded RNA that is complementary to an mRNA sequence encoding a protein having s-CPG15 biological activity.

35. The method of claim 34, wherein said double-stranded RNA is processed into small interfering RNAs (siRNAs) 19 to 25 nucleotides in length.

36. The method of claim 35, wherein said siRNA comprises the sequence of
SEQ ID NO: 2.

37. The method of claim 35, wherein said siRNA comprises the sequence of
5 SEQ ID NO: 3.

38. A method of enhancing cell death, said method comprising
administering to a cell a nucleic acid encoding a truncated form of CPG15, wherein said
administering is sufficient to reduce or inhibit the biological activity of s-CPG15.

10

39. A method of enhancing cell death, said method comprising
administering to a cell a compound comprising a truncated form of CPG15 protein,
wherein said administering is sufficient to reduce or inhibit the biological activity of s-
CPG15.

15

40. The method of any one of claims 33, 34, 39, and 38, wherein said cell
death is increased by at least 5%.

41. A composition of matter comprising a purified antibody or antigen-
20 binding fragment thereof that specifically binds s-CPG15.

42. A composition of matter comprising an siRNA that is complementary to
an mRNA sequence encoding s-CPG15.

25 43. A method of manufacturing s-CPG15 comprising expressing said s-
CPG15 protein in a population of cells and isolating from the supernatant of said cell
population said s-CPG15.

44. The method of claim 43, wherein said s-CPG15 is at least 85% pure.

45. The method of claim 43, wherein said s-CPG15 comprises less than 20% CPG15.

5 46. The method of claim 43, wherein said s-CPG15 comprises a post-translational modification.

47. The method of claim 46, wherein said post-translational modification comprises the attachment of a membrane component to said s-CPG15.

10 48. The method of claim 43, wherein said cells are neuronal cells or hippocampal cells.

49. The method of claim 43, wherein said cells are selected from the group
15 consisting of COS cells, CV-1 cells, L cells, C127 cells, 3T3 cells, CHO cells, HeLA cells, 293 cells, 293T cells, and BHK cells.

50. A method of identifying a candidate compound that modulates cell death, cell survival, or cellular differentiation pathways, said method comprising the steps
20 of

(a.) mixing s-CPG15 with a test mixture,
(b.) identifying a candidate compound in said mixture that interacts with said s-CPG15.

25 51. The method of claim 50, further comprising the step after step (a) of incubating said s-CPG15/test mixture with an insoluble affinity support reagent that specifically binds s-CPG15.

52. The method of claim 51, further comprising the step of recovering said affinity support reagent bound to CPG15.

53. The method of claim 50, wherein said mixture is a cell lysate.

54. The method of claim 50, wherein said mixture is a lysate from a tissue.

55. The method of claim 50, wherein said modulation comprises an increase said cell death, cell survival, or cellular differentiation pathways.

56. The method of claim 55, wherein said increase is at least 5%.

57. The method of claim 50, wherein said modulation comprises a decrease in said cell death, cell survival, or cellular differentiation pathways.

58. The method of claim 57, wherein said decrease is at least 5%.